REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated January 11, 2006 are respectfully requested. Claims 1-3 and 46-52 are pending.

I. Amendments

Figs. 2 and 3 are amended to correct the element indicated by numerical identifier 14. Basis for the correction is found in Fig. 1 where element 14 is correctly indicated.

Claims 40-46 stand canceled without prejudice to Applicants' right to pursue the subject matter in a continuing application.

II. Rejection Under 35 U.S.C. § 103

Claims 1-3 and 46-52 were rejected under 35 U.S.C. §103 as allegedly obvious over WO 00/09184 ("'184") in view of Kheiri *et al.*, U.S. Patent No. 6,364,889 ("Kheiri"). This rejection is respectfully traversed for the following reasons.

The Examiner alleges that the "velocity along with the disclosed mass of the needle and moving parts...will result in the claimed energy on impact of 0.05-3 Joules/cm^2." (January 11, 2006 Office action, page 2). Applicants respectfully submit that this analysis is in error and that a prima facie case of obviousness has not been established.

The '184 document discloses a needle velocity of 1-100 m/s (page 2, lines 15-16) and a needle and moving parts mass of between 0.01-2.5 grams (page 5, line 1). Kinetic energy (KE) is calculated using the equation $KE = ½m•v^2$ (see Applicants' application paragraph [00027]). Thus, the kinetic energy, based on the velocity (v) and mass (m) values disclosed in the '184 application, is between 5 x 10^{-6} J[(1)] and 12.5 J[(2)], thus an energy range that spans seven (7) orders of magnitude.

Notably, as illustrated by the calculations in the preceding paragraph, disclosure of the velocity and mass do *not* permit calculation of an energy *density* (i.e. Joules/cm^2), as alleged by the Examiner, but merely arrive at an energy value (i.e., Joules). In fact, the '184 disclosure is completely silent with respect to a suitable area over which the energy should be transmitted. One can speculate that the area is the tip of the single needle or perhaps the sum of the tip areas of the multiple needles in the embodiment shown in Fig. 5, but no guidance in the '184 document is given. One can also speculate that if the estimated area of a single needle tip is

---

[1]KE = 1/2 (0.01 gm)(1 m/s)^2 = 0.005 g•m^2/s^2= 5 x 10^{-6} kg•m^2/s^2 = 5 x 10^{-6} Nm = 5 x 10^{-6} J

[2] KE = 1/2 (2.5 g)(100 m/s)^2 = 12,500 g•m^2/s^2= 12.5 kg•m^2/s^2 = 12.5 Nm = 12.5 J

0.008 cm^{2}[3], the corresponding energy density might be calculated to be in the range of 6.2 x 10^{-4} J[4] to 1602.6 J/cm^{2}[5]. This energy density still spans seven orders of magnitude, and while such a broad range may or may not be suitable for penetration of single needle, clearly no guidance is given as to what energy density is suitable for penetration of an array of microneedles. Given the complete lack of guidance in the '184 document regarding a suitable area for transmission of the very large range of possible energies, it cannot be said that the '184 document teaches the energy density set forth in the pending claims.

More importantly, the pending claims actually recite a *power*[6] density, since a time of less than about 10 milliseconds (ms) in which the energy density is applied is stated. As noted in the earlier-submitted Stone Declaration, application of an agent from the microprotrustion member with the claimed power density provides (i) an increased rate of delivery of the agent and (ii) a more uniform and consistent puncture depth across the microprotrusion array. Applicants have clearly established in Example 2 and Fig. 7 that these benefits were not observed at lower power densities[7]. Thus, the claimed energy density provides meaningful and measurable benefits.

The Examiner points to the Kheiri document to provide the claimed time element. Again the Examiner is mistaken in the analysis. Kheiri describes an electronic device for lancing the skin. In the Kheiri device, a voltage source provides sufficient current through a voice coil to propel the lancet out of the device (the "out-stroke") in 7 ms or less (Col. 6, lines 60-63). Retraction of the lancet from the skin back into the device (the "in-stoke") is controlled by a second timing circuit and occurs over a 10-15 ms time period (Col. 7, line 52). The Examiner combines the 10 ms "in-stroke" motion, when the lancet is retracted from the puncture site back into the device, with the "energy" calculation based on the velocity and mass of the '184 device for puncturing the skin. This makes no sense. The 10 ms time interval corresponds to *withdrawal* of the lancet from the skin (see Kheiri Col. 7, lines 41-43), yet the calculated energy is for a velocity and mass of a needle for *puncturing* the skin.

Further, even if the Examiner were to combine the 7 ms time interval of the out-stroke of the Kheiri device, there is no basis for picking a 7 ms time over any other time taught in the

---

[3]Based on an assumption that the needle tip diameter is 1 mm (0.1 cm), then since $A=\pi r^2$ = 3.14•(0.05 cm^2)=0.0078 cm^2

[4]5 x 10^{-6} J/0.0078 cm^2 = 6.2 x 10^{-4} J/cm^2

[5]12.5 J/0.0078 cm^2 = 1602.6 J/cm^2

[6]Power = energy (J) /time (sec).

[7]In Example 2, manual pressure of 0.2 kg/cm^2 corresponds to 0.2 J/cm^2, since there are 0.10 J/kg. Thus, the power density for manual pressure was 0.04 J/cm^2•sec (0.2/5). The power density for the impact applicator was 20 J/cm^2•sec (0.2/.01).

prior art, other than the guidance provided in Applicants' claim. The importance of the time over which the energy density is transmitted is illustrated in Example 2 of the instant application, where an energy density of 0.2 J/cm^2 was applied to skin over a 5 second period or over a 10 millisecond period, corresponding to power densities of 0.04 J/cm^2•sec and 20 J/cm^2•sec, respectively. The higher energy density at the correspondingly shorter delivery time of 10 milliseconds provided a higher delivery of model drug (ovalbumin) as seen in Fig. 7.

In summary, the combination of the '184 document with Kheiri fails to show or suggest the claimed power density. The '184 document does not teach the recited energy density, but merely teaches a spectacularly large energy range, as illustrated by the calculations above. No guidance is given in the '184 document or in Kheiri of an area over which this energy should be transmitted for delivery of an agent from an array of microprotrusions. Furthermore, combination of a 10 ms "in-stroke" that corresponds to *withdrawal* of a needle from the skin with an energy range for *puncturing* the skin makes no sense and is a classic example of "picking and choosing" features from the art to arrive at the claimed elements.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

III. Conclusion

In view of the above amendments and remarks, applicants submit that claims * are in condition for allowance. Therefore, a Notice of Allowance is respectfully requested. If the Examiner believes a telephone conference would expedite the prosecution of the present application, the Examiner is encouraged to call the undersigned at (650) 564-5887.

Respectfully submitted,

Michael Atkins

Date: 4/11/06

Michael Atkins
Registration No. 35,431

Correspondence Address:
Customer No. 27777

Amendments to the Drawings:

Enclosed herewith are amended versions of Figure 2 and of Figure 3, in which the element indicated by numerical identifier 14 is amended for consistency with Figure 1. Submitted herewith are amended drawing sheets identified in the header as a "Replacement Sheet."